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New Form of Platyspondylic Lethal Chondrodysplasia

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We report on a sporadic case of a hitherto unknown lethal skeletal dysplasia. The cardinal clinical manifestations consisted of frontal bossing, cloudy corneae, low nasal ridge, and micrognathia, hypoplastic thorax, and rhizomelic micromelia. Laryngoscopy and neck CT disclosed laryngeal stenosis, and brain CT demonstrated hypoplasia of the corpus callosum. Skeletal survey demonstrated hypoplasia of facial bones and short skull base, extremely severe platyspondyly, hypoplastic ilia, and delayed epiphyseal ossification and rhizomelic shortness of tubular bones. The long bones appeared overtubulated with exaggerated metaphyseal flaring. The humeri were particularly short and bowed. Bowing of the radii and ulnae with subluxation of radial heads presented as a Madelung-like deformity. Unlike the long bones, the short tubular bones were not short and normally modeled. The skeletal changes were superficially similar to those in a group of lethal platyspondylic chondrodysplasias, but were inconsistent with any known subtypes of this group or other lethal skeletal dysplasias. © 1996 Wiley-Liss, Inc.

KEY WORDS: osteochondrodysplasia, severe platyspondyly, cloudy cornea, laryngeal stenosis

INTRODUCTION

Lethal osteochondrodysplasias comprise a heterogeneous group of disorders [Spranger and Maroteaux, 1990]. In addition to well-known entities which have been thoroughly elucidated, a number of isolated cases with atypical clinical and radiological findings have been described, which defy the proper classification of lethal skeletal dysplasias [Langer et al., 1983; Burn et al., 1986; Silence et al., 1987]. Further case documentation is necessary in these atypical cases to group similar cases or distinguish them. We recently encountered a sporadic case of lethal skeletal dysplasia that was inconsistent with any established disorders. The clinical and radiological manifestations of this patient are described here, and the differential diagnosis is discussed.

CLINICAL REPORT

The patient was a Japanese boy born at 38 weeks of gestation to healthy and unrelated parents. Micromelia had been noted by ultrasonography at 28 weeks of gestation. His gravida 2 para 0 mother was 39 years old and his father 34 years old at the birth of the patient. Birth weight was 2,064 g, length 36 cm, occipitofrontal circumference (OFC) and chest circumference 31 cm. Apgar scores were 7 and 8 at 1 min and 5 min, respectively. He had no clinical symptoms until 4 days, but thereafter he started to show cyanosis and tachypnea. At age 21 days he was transferred to our hospital. On admission, he weighed 1,985 g and showed inspiratory dyspnea with retraction. He had cyanotic and icteric skin, flat anterior fontanel, bilateral cloudy cornea, frontal bossing, low nasal ridge, micrognathia, short limbs, and short neck (Fig. 1). The liver was tender and palpable 1 cm below the costal margin and the spleen was not palpable. Heart sounds were normal. Laryngoscopic examination and neck CT scan showed a narrow larynx. Normal results were obtained for red blood cell count, hemoglobin, platelet count, serum sodium, serum potassium, serum calcium, serum phosphate, blood urea nitrogen, serum creatinine, total protein, albumin, serum alanine aminotransferase, alkaline phosphatase, serum free T_3, free T_4, and TSH. Abnormal laboratory findings were as follows: white blood cell count was 20,900/mm^3, serum aspartate aminotransferase 65 IU/l, serum lactate dehydrogenase 836 IU/l, creatinine phosphokinase 404 IU/l, and total bilirubin 11.2 μmol/l. Chromosome analysis demonstrated a normal male karyotype of 46,XY. Urinalysis showed no hematuria and proteinuria. Urinary excretion of mucopolysaccharide was normal.

Radiological examination demonstrated hypoplasia of facial bones, short skull base, extremely severe

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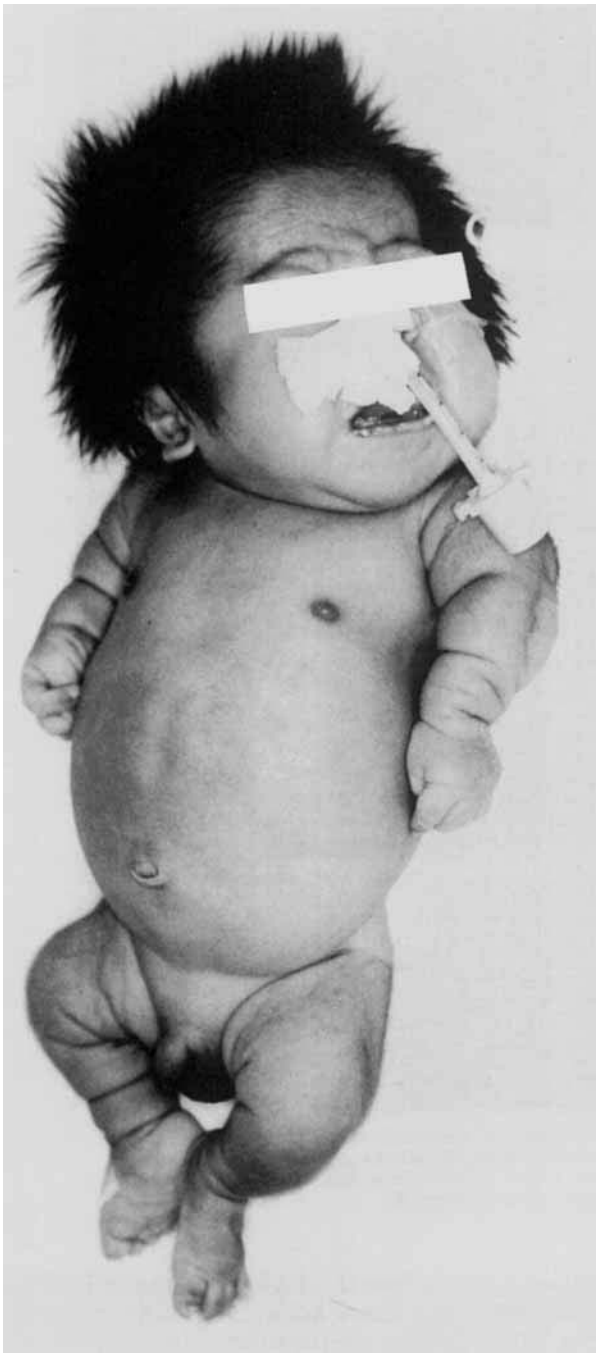

Fig. 1. Photograph of the patient.

platyspondyly, hypoplastic ilia, rhizomelic shortness of long bones, and delayed epiphyseal ossification. The long bones appeared rather overtubulated with exaggerated metaphyseal flare (Fig. 2). The humeri were particularly short and bowed. The intercondylar notches of distal humeri appeared deep. The radii and ulnae appeared bowed with subluxation of radial heads, resulting in a Madelung-like deformity. Unlike the long bones, the short tubular bones were not short and normally modeled (Fig. 2). An echocardiogram showed a left ventricular ejection fraction of 0.70 and left-to-right shunting through patent ductus arteriosus (2.5 mm in diameter). Brain CT did not show ventricular dilatation, but rather hypoplasia of the corpus callosum. He was being tube fed and intubation relieved temporalily his dyspnea and cyanosis. Nevertheless, his respiration gradually worsened, and he died of respiratory insufficiency at age 43 days. Autopsy was not performed.

DISCUSSION

Since lethal skeletal dysplasias generally share common findings, such as frontal bossing, midface hypoplasia, hypoplastic thorax, protuberant abdomen, and severe rhizomelic shortness of the limbs, diagnosis of these disorders primarily relies on radiological findings. Pathological examination may address heterogeneity of disorders whose manifestations may be radiologically indistinguishable, as exemplified in platyspondylic lethal chondrodysplasia type Torrance and type San Diego. Although an autopsy specimen was not available from the present patient, in this paper we focus on the radiological differential diagnosis between the disorder afflicting this patient and other lethal skeletal dysplasias.

The radiological findings of our patient differ from those in common lethal bone dysplasias, such as thanatophoric dysplasia, achondrogenesis, and lethal osteogenesis imperfecta. A number of disorders which Spranger grouped together and designated as lethal platyspondylic chondrodysplasias [Spranger and Maroteaux, 1990], i.e., Torrance type, San Diego type, Luton type, Sedaghatian or Shiraz type, and opsismodysplasia, are the most important disorders to be differentiated from the present disorder. The Torrance type and San Diego type platyspondylic lethal chondrodysplasias are histologically distinct but radiologically identical disorders. The radiological hallmarks of these disorders, including wafer-thin vertebral bodies, hypoplastic ilia, severe rhizomelia particularly of the humeri, delayed epiphyseal ossification, relatively long short tubular bones, and bowed radii, overlap with those of the present patient. However, these two disorders exhibit extreme shortness of the long bones manifesting as rectangular shape and ragged metaphyseal ends, which contrast with the short, but somewhat thin, long bones and smooth metaphyseal ends in the present patient. The radiological findings in the Luton type are similar to but milder in degree of platyspondyly and limb shortness less than those of the Torrance and the San Diego type, and somewhat resemble the changes in our patient. Nevertheless, the Luton type is manifested by straight radii and ulnae and by long bones thicker than those observed in our patient. The Sedaghatian type is the radiologically mildest form of lethal platyspondylic chondrodysplasia. The skeletal changes in this disorder are distinguishable from those in our patient: the ragged metaphyseal ends and moderate platyspondyly in the Sedaghatian type do not resemble the smooth metaphyseal ends and severe

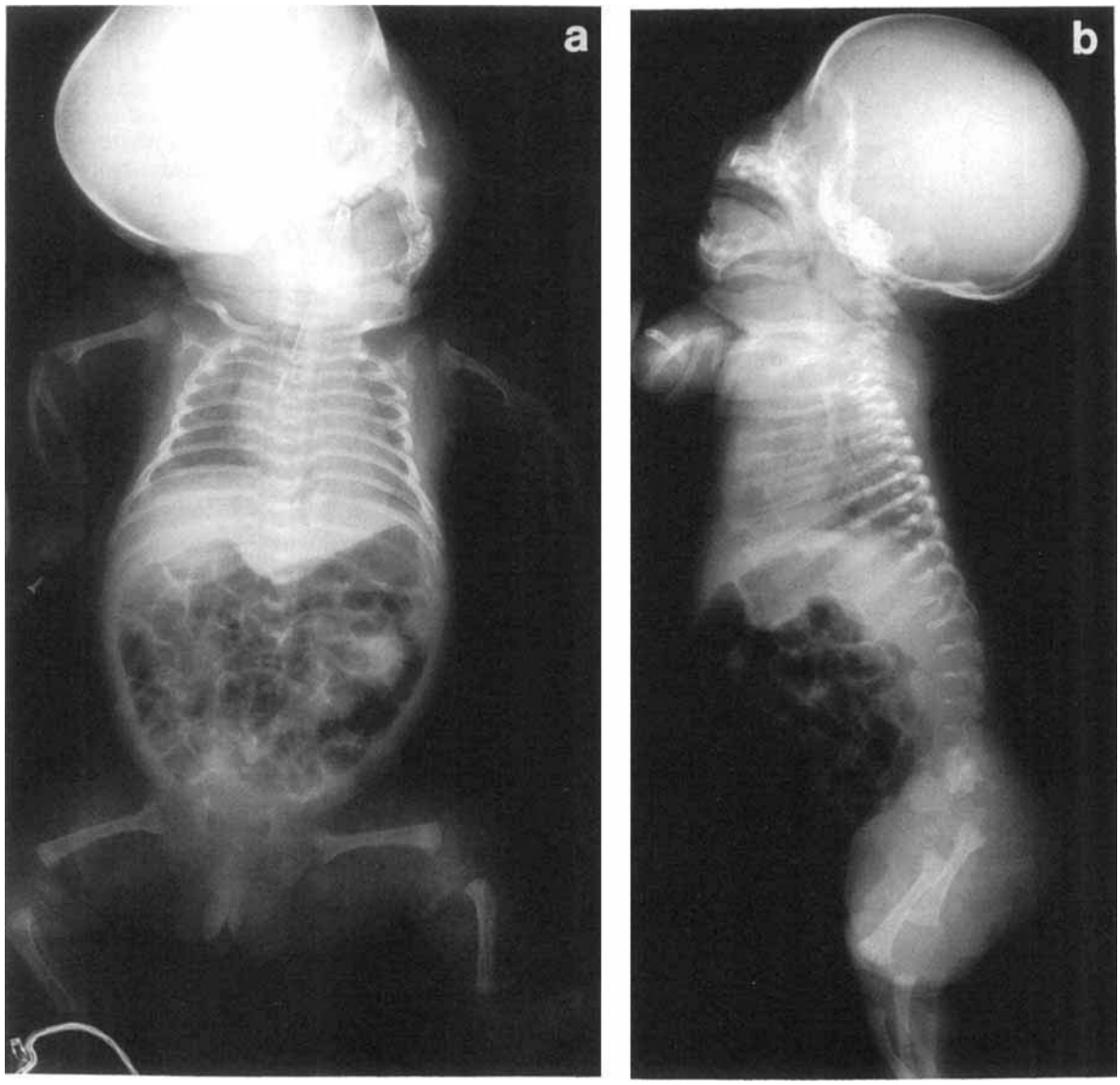

Fig. 2. Skeletal radiographs. Note narrow thorax with thin ribs, rhizomelic shortness and overtubulation of the long bones (**a**), short skull base and severe platyspondyly (**b**), short and broad ilia with short greater sciatic notch and metaphyseal flaring of the femora (**c**), and deep intercondylar notches of the distal humerus, bowed humerus and Madelung-like deformity of the forearm (**d**).

platyspondyly in our patient. Opsismodysplasia is not obligatorily lethal in the neonate in contrast to the outcome for our patient as well as for other types of platyspondylic lethal chondrodysplasias, although a fatal outcome related to respiratory infections generally ensues during early childhood. The radiological changes in opsismodysplasia are also distinct from those in our patient in several respects, i.e., platyspondyly is more pronounced in opsismodysplasia, and very stubby short tubular bones in opsismodysplasia are distinct from relatively long short tubular bones in our patient. Of the other rare cases which Spranger grouped with platyspondylic lethal chondrodysplasia, none matched the features of the present patient.

Deep intercondylar notches of the distal humeri in our patient remind us of the "bifid distal humeri" in atelosteogenesis type II, which was reported by Sillence et al. [1987], and is now known as McAlister dysplasia. This lethal disorder shares some anomalies with those of our patient: Madelung-like deformity and platyspondyly. However, the absence of cleft lip and/or palate, hitchhiker's thumb and wide separation between the first and second toes in our patient ultimately precludes the possibility of McAlister dysplasia.

Cloudy corneae and laryngeal stenosis are extremely rare symptoms of lethal and/or semilethal skeletal dysplasias. Cloudy corneae are observed in the brachymesomelia-renal syndrome, which is a lethal mesomelic dysplasia associated with renal cysts reported by Langer et al. [1983]. Laryngeal stenosis complicates thoracolaryngopelvic dysplasia, a semilethal condition resembling asphyxiating thoracic dysplasia [Burn

Fig. 2. *(Continued.)*

et al., 1986]. However, the disorder in the present patient is easily distinguished from these disorders.

In conclusion, the overall picture of the present patient does not completely fulfill the diagnostic characteristics of any known lethal skeletal dysplasias. On the basis of the radiological resemblance, we tentatively classify the present case as a new form of platyspondylic lethal chondrodysplasia.

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